

IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0486/001/001

Case No: 2029180

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Innovata Biomed Ltd

1 Mere Way, Ruddington, Nottingham, NG11 6JS, United Kingdom

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Clickhaler Salbutamol inhalation powder, 95 micrograms/inhalation

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **27/08/2008**.

Signed on behalf of the Irish Medicines Board this

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Clickhaler Salbutamol inhalation powder, 95 micrograms/inhalation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered actuation of 3 mg of inhalation powder contains 114 micrograms of salbutamol sulphate (95 micrograms salbutamol base) and delivers 110 micrograms of salbutamol sulphate (90 micrograms of salbutamol base).

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder.

A plastic inhaler device incorporating an actuating and metering mechanism enclosed within an aluminium foil heat sealed bag.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Clickhaler Salbutamol is indicated for the symptomatic treatment of bronchospasm in bronchial asthma and other conditions with associated reversible airways obstruction. Appropriate anti-inflammatory therapy should be considered in line with current practice.

Clickhaler Salbutamol may be used when necessary to relieve attacks of acute dyspnoea due to bronchoconstriction.

Clickhaler Salbutamol may also be used before exertion to prevent exercise-induced bronchospasm or before exposure to a known unavoidable allergen challenge.

4.2 Posology and method of administration

Adults: For the relief of acute bronchospasm and for managing intermittent episodes of asthma, one inhalation may be administered as a single dose; this may be increased to two inhalations if necessary. If the response is inadequate, higher doses than two inhalations can be used. The maximum recommended dose is two inhalations three or four times a day.

To prevent exercise-induced bronchospasm one or two inhalations should be taken 15 minutes before exertion.

One or two inhalations may also be taken before foreseeable contact with allergens.

Elderly: as for adults

Children: One inhalation is the recommended dose for the relief of acute bronchospasm, in the management of episodic asthma or before exercise. If the response is inadequate, higher doses than one inhalation can be used.

On demand use should not exceed four times daily. The bronchodilator effect of each administration of inhaled salbutamol lasts for at least four hours except in patients whose asthma is becoming worse. Such patients should be warned not to increase their usage of the inhaler, but should seek medical advice since treatment with, or an increased dose of an inhaled and/or systemic glucocorticosteroid is indicated.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

The following instructions for use are included in the Patient Information Leaflet:

1. Remove mouthpiece cover from the inhaler
2. Shake the inhaler well
3. Hold the inhaler upright with thumb on the base and finger on the push button. Press the dosing button down firmly - once only
4. Breathe out as far as is comfortable.
Note: do not blow into the device at any time.
5. Place mouthpiece in your mouth. Close lips firmly around it (do not bite it)
6. Breathe in through your mouth steadily and deeply, to draw the medicine into your lungs.
7. Hold your breath, take the inhaler from your mouth and continue holding your breath for about 5 seconds.
8. For the second puff, keep the inhaler upright and repeat steps 2-7.
9. Replace the mouthpiece cover.

4.3 Contraindications

Clickhaler Salbutamol is contraindicated in patients with hypersensitivity (allergy) to any of the active substances or the excipients (see section 6.1 List of Excipients).

4.4 Special warnings and precautions for use

Bronchodilators should not be the only or main treatment in patients with moderate to severe or unstable asthma. Severe asthma requires regular medical assessment including lung function testing as patients are at risk of severe attacks and even death. Physicians should consider using the maximum recommended dose of inhaled corticosteroid and/or oral corticosteroid therapy in these patients. Increasing use of bronchodilators, in particular short-acting inhaled beta-2-agonists to relieve symptoms, indicates deterioration of asthma control. If patients find that short-acting bronchodilator treatment becomes less effective or they need more inhalations than usual, they should be warned by the prescriber of the need for consulting immediately. In this situation, patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy (eg. higher doses of inhaled corticosteroids or a course of oral corticosteroids).

Salbutamol should be administered cautiously, especially with systemic therapy, to patients suffering from thyrotoxicosis, myocardial insufficiency, hypertension, known aneurysms, decreased glucose tolerance, manifest diabetes, phaeochromocytoma and concomitant use of cardiac glycosides. Caution should also be applied in patients with myocardial ischemia, tachyarrhythmias and hypertrophic obstructive cardiomyopathy.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Salbutamol and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together.

Potentially serious hypokalaemia has resulted from systemic β_2 -agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

4.5 Interaction with other medicinal products and other forms of interaction

Salbutamol and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together. Caution is also advised in patients using cardiac glycosides.

Potentially serious hypokalaemia has resulted from systemic β_2 -agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia.

Patients should be instructed to discontinue salbutamol at least 6 hours before intended anaesthesia with halogenated anaesthetics, wherever possible.

4.6 Pregnancy and lactation

Pregnancy: Administration of salbutamol during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus. As with the majority of drugs there is little published evidence of its safety in the early stages of pregnancy, but in animal studies, there was evidence of some harmful effects in the fetus at very high dose levels.

Lactation: Salbutamol may be secreted in breast milk. It is not known whether salbutamol has a harmful effect on the neonate and so its use should be restricted to situations where it is felt that the expected benefit to the mother is likely to outweigh any potential risk to the neonate.

4.7 Effects on ability to drive and use machines

Individual reactions, especially at higher doses, may be such that patients' ability to drive or use machines may be affected, particularly so at the beginning of treatment and in conjunction with alcohol.

The possible side effects of salbutamol such as transient muscle cramps and tremor may necessitate caution when using machines.

4.8 Undesirable effects

The side effects are dose dependent and due to the direct mechanism of β_2 -agonists.

Hypersensitivity reactions include angioedema and urticaria, bronchospasm, hypotension and collapse and have been reported very rarely.

Blood and the lymphatic system disorders: potentially serious hypokalaemia may result from systemic β_2 -agonist therapy. Special precautions should be taken in patients using β_2 -agonists with hypokalaemia because of the increased risk of tachycardia and arrhythmias. Hypokalaemia may be potentiated by concomitant therapy with corticosteroids, diuretics and xanthines.

Psychiatric disorders: nervousness, feeling of tenseness. As with other β_2 agonists, hyperactivity in children has been reported rarely.

Nervous system disorders: mild tremor, headache, dizziness.

Cardiac disorders: tachycardia, angioedema, hypotension, cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) and myocardial ischemia (see Section 4.4) have been reported in association with β_2 agonists, usually in susceptible patients.

Respiratory, thoracic and mediastinal disorders: as with other inhalation therapy, the potential for paradoxical bronchospasm should be kept in mind. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

Gastrointestinal disorders: nausea

Skin and subcutaneous tissue disorders: urticaria.

Musculoskeletal, connective tissue and bone disorders: there have been rare reports of transient muscle cramps

General disorders and administration site conditions: oral and pharyngeal irritation can occur.

4.9 Overdose

An overdose should be treated symptomatically.

The preferred antidote for overdosage with salbutamol is a cardioselective beta-blocking agent but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

If hypokalaemia occurs potassium replacement via the oral route should be given. In patients with severe hypokalaemia intravenous replacement may be necessary.

Increased serum lactate levels, and rarely, lactic acidosis, have been reported following therapy with salbutamol, particularly after high dose administration. Symptoms include deep, rapid breathing, cold and blue coloured fingers and toes, inability to concentrate and general malaise.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: R03A C02

Salbutamol is a beta-adrenergic stimulant which has a selective action on bronchial β_2 -adrenoceptors at therapeutic doses. Following inhalation, salbutamol exerts a stimulating action on β_2 receptors on bronchial smooth muscles, and thus ensures rapid bronchodilation which becomes significant within a few minutes and persists for 4 to 6 hours.

The drug also causes vasodilation leading to a reflex chronotropic effect and widespread metabolic effects, including hypokalaemia.

5.2 Pharmacokinetic properties

Following treatment with salbutamol by inhalation, only approximately 10% or less of the drug is deposited in the airways and the remainder is swallowed. Pre-systemic metabolism of salbutamol is considerable and occurs primarily in the gastrointestinal tract and by conjugation to form an inactive sulphate ester. The systemic clearance for salbutamol is 30 l/hr. Salbutamol is eliminated both through excretion of unchanged drug in urine and through metabolism mainly via sulphate conjugation.

The elimination half-life varies between 3 and 7 hours. Salbutamol is well absorbed from the gastrointestinal tract.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity. Findings concerning teratogenicity in rabbits at high systemic exposure and the induction of benign mesovarian leiomyomas in rats are not considered of clinical concern.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (which contains milk protein)

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

2 years in unopened foil pouch. 6 months when removed from foil patch.

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package.

6.5 Nature and contents of container

A plastic inhaler device incorporating an actuating and metering mechanism enclosed within an aluminium foil heat sealed bag. Each device contains 750mg of powder – sufficient for 200 actuations.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Instructions for use are included in the patient information leaflet. These are also included in Section 4.2.

7 MARKETING AUTHORISATION HOLDER

Innovata Biomed Ltd
1 Mere Way
Ruddington
Nottingham
NG11 6JS
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 486/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th April 1998

Date of last renewal: 8th May 2007

10 DATE OF REVISION OF THE TEXT

August 2008